

What is claimed is:

1. An isolated nucleic acid molecule, comprising a sequence selected from the group consisting of: (a) the sequence of SEQ ID NO:1 ; and (b) the sequence fully complementary to (a).

5 2. The nucleic acid molecule of Claim 1, wherein said nucleic acid molecule is less than about 5 kilobases in length.

3. The nucleic acid molecule of Claim 1, wherein said nucleic acid molecule is less than about 70 nucleotides in length.

10 4. A nucleic acid molecule of Claim 1, wherein said molecule comprises SEQ ID NO:1.

5. An isolated nucleic acid molecule which comprises at least one base variation from that of the human CYP3A4 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

(a) a nucleic acid molecule that comprises a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene and at least 17 other bases of said CYP3A4 gene contiguously appurtenant to said position; and

(b) a nucleic acid molecule which is fully complementary to a nucleic acid molecule of (a).

6. The nucleic acid molecule of Claim 5, wherein said nucleic acid molecule is less than about 5 kilobases in length.

7. The nucleic acid molecule of Claim 5, wherein said nucleic acid molecule is less than about 70 nucleotides in length.

8. A nucleic acid molecule of Claim 5, wherein said molecule comprises a sequence selected from the group consisting of SEQ ID NO:1, and a nucleic acid sequence which is fully complementary to SEQ ID NO:1.

9. An isolated nucleic acid molecule, comprising a sequence selected from the group consisting of: (a) the sequence of SEQ ID NO:2; and (b) the sequence fully complementary to (a).

10. The nucleic acid molecule of Claim 9, wherein said nucleic acid molecule  
5 is less than about 5 kilobases in length.

11. The nucleic acid molecule of Claim 9, wherein said nucleic acid molecule is less than about 70 nucleotides in length.

12. A nucleic acid molecule of Claim 9, wherein said molecule comprises  
SEQ ID NO:2.

13. An isolated nucleic acid molecule which comprises at least one base variation from that of the human CYP3A5 sequence, wherein said nucleic acid molecule is selected from the group consisting of:

(a) a nucleic acid molecule that comprises an A nucleotide for a G nucleotide at position-147 of the promoter of said CYP3A5 gene with respect to the start codon of said CYP3A5 gene and at least 33 other bases of said CYP3A5 gene contiguously appurtenant to said position; and

(b) a nucleic acid molecule which is fully complementary to a nucleic acid molecule of (a).

14. The nucleic acid molecule of Claim 13, wherein said nucleic acid molecule is less than about 5 kilobases in length.

15. The nucleic acid molecule of Claim 13, wherein said nucleic acid molecule is less than about 70 nucleotides in length.

16. A nucleic acid molecule of Claim 13, wherein said molecule comprises a sequence selected from the group consisting of SEQ ID NO:2, and a nucleic acid sequence which is fully complementary to SEQ ID NO:2.

17. A method of detecting a variant gene having a polymorphism associated with reduced metabolism of a substrate selected from the group consisting of a CYP3A4 substrate, a CYP3A5 substrate and a GSTM1 substrate in an individual, said method comprising:

5 (a) obtaining a nucleic acid sample comprising a gene isolated from said individual, said gene selected from the group consisting of a CYP3A4 gene, a CYP3A5 gene and a GSTM1 gene; and,

(b) detecting the presence or absence in said individual of a polymorphism selected from the group consisting of (i) a substitution of a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene, wherein the presence of said substitution is associated with reduced CYP3A4 substrate metabolism: (ii) a substitution of a G nucleotide for an A nucleotide at position-147 of the promoter of said CYP3A5 gene, wherein the presence of said substitution is associated with reduced CYP3A5 substrate metabolism: and (iii) a GSTM1 null mutation, wherein the presence of said GSTM1 null mutation is associated with reduced GSTM1 substrate metabolism.

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18. The method of Claim 17, wherein said method further comprises, for an individual having one of said nucleic acid sequences, determining whether said individual is homozygous or heterozygous for the polymorphism.

20 19. The method of Claim 17, wherein the step of detecting is selected from the group consisting of a cDNA assay and a genomic DNA assay

20. The method of Claim 17, wherein said method comprises the step of

digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence comprising said polymorphism and the corresponding wildtype sequence.

21. The method of Claim 17, wherein said step of detecting comprises  
5 amplifying a selected region of the nucleic acid molecule of the individual.

22. The method of Claim 17, wherein said gene is a CYP3A4 gene and wherein said CYP3A4 substrate is selected from the group consisting of cyclophosphamide and BCNU.

23. The method of Claim 17, wherein said gene is a CYP3A5 gene and  
10 wherein said CYP3A5 substrate is selected from the group consisting of cyclophosphamide and BCNU.

24. The method of Claim 17, wherein said gene is a GSTM1 gene and wherein said GSTM1 substrate is selected from the group consisting of cyclophosphamide and BCNU.

25. A method for selecting a treatment for a cancer patient, said method comprising:
- (a) obtaining a nucleic acid sample comprising a gene isolated from said individual, said gene selected from the group consisting of a CYP3A4 gene, a CYP3A5 gene and a GSTM1 gene;
- (b) detecting the presence or absence in said individual of a polymorphism selected from the group consisting of (i) a substitution of a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene, wherein the presence of said substitution is associated with reduced CYP3A4 substrate metabolism: (ii) a substitution of a G nucleotide for an A nucleotide at position-147 of the promoter of said CYP3A5 gene, wherein the presence of said substitution is associated with reduced CYP3A5 substrate metabolism: and (iii) a GSTM1 null mutation, wherein the presence of said GSTM1 null mutation is associated with reduced GSTM1 substrate metabolism; and
- (c) selecting a cancer treatment regime that does not include administration of an anti-cancer agent selected from the group consisting of cyclophosphamide and BCNU if one or more of said polymorphisms are present.

26. The method of Claim 25, wherein said method further comprises, for an individual having one of said polymorphisms, determining whether said individual is homozygous or heterozygous for the polymorphism.

27. The method of Claim 25, wherein the step of detecting is selected from the group consisting of a cDNA assay and a genomic DNA assay.

28. The method of Claim 25, wherein said method comprises the step of digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence comprising said polymorphism and the corresponding wildtype sequence.

5 29. The method of Claim 25, wherein said step of detecting comprises amplifying a selected region of the nucleic acid molecule of the individual.

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30. A method for selecting a treatment for a cancer patient, said method comprising:

(a) obtaining a nucleic acid sample comprising a CYP3A4 gene, a CYP3A5 gene and a GSTM1 gene;

5 (b) detecting the presence or absence in said individual of the following polymorphisms (i) a substitution of a G nucleotide for an A nucleotide at position -392 of the promoter of said CYP3A4 gene with respect to the start codon of said CYP3A4 gene, wherein the presence of said substitution is associated with reduced CYP3A4 substrate metabolism: (ii) a substitution of a G nucleotide for an A nucleotide at position-147 of the  
10 promoter of said CYP3A5 gene, wherein the presence of said substitution is associated with reduced CYP3A5 substrate metabolism: and (iii) a GSTM1 null mutation, wherein the presence of said GSTM1 null mutation is associated with reduced GSTM1 substrate metabolism; and

(c) selecting a cancer treatment regime that does includes administration of an  
15 anti-cancer agent selected from the group consisting of cyclophosphamide and BCNU if none of said polymorphisms are present.

31. The method of Claim 30, wherein said method further comprises, for an individual having one of said polymorphisms, determining whether said individual is homozygous or heterozygous for the polymorphism.

20 32. The method of Claim 30, wherein the step of detecting is selected from the group consisting of a cDNA assay and a genomic DNA assay.

33. The method of Claim 30, wherein said method comprises the step of

digesting a nucleic acid molecule with a restriction enzyme that distinguishes between said nucleic acid sequence comprising said polymorphism and the corresponding wildtype sequence.

34. The method of Claim 30, wherein said step of detecting comprises
- 5 amplifying a selected region of the nucleic acid molecule of the individual.

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